Rethinking Reproduction

Past and future of in vitro gametogenesis (IVG)

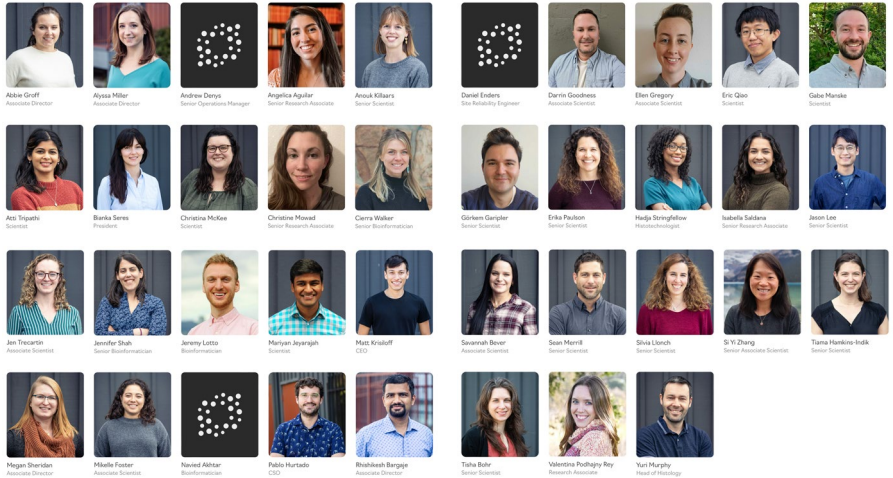
Pablo Hurtado Gonzalez

Conflict of interest

I’m co-founder and CSO at Conception

Conception

- 40 scientist working full time
- State-of-the-art facilities
- $40+MM raised so far



Let’s dive in the world of in vitro gametogenesis (IVG)

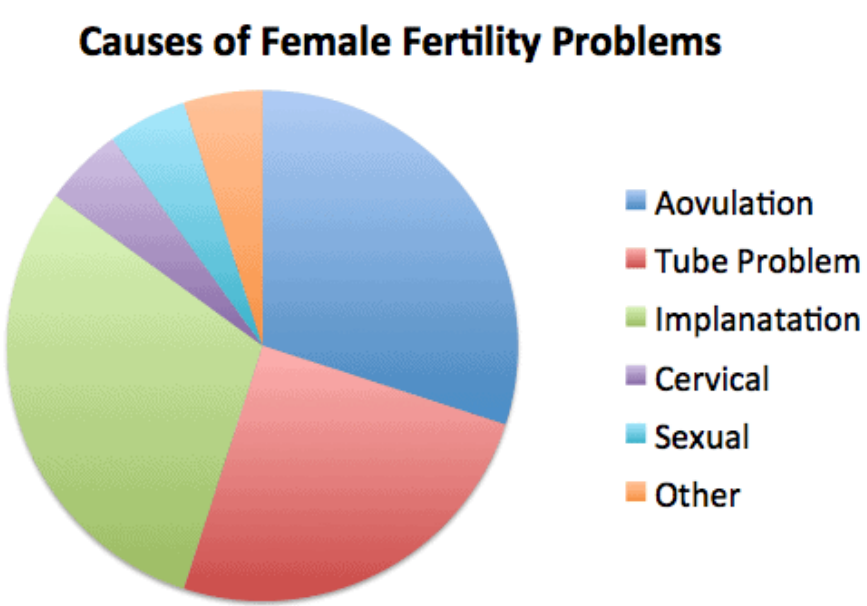
Needs Assessment Statement:

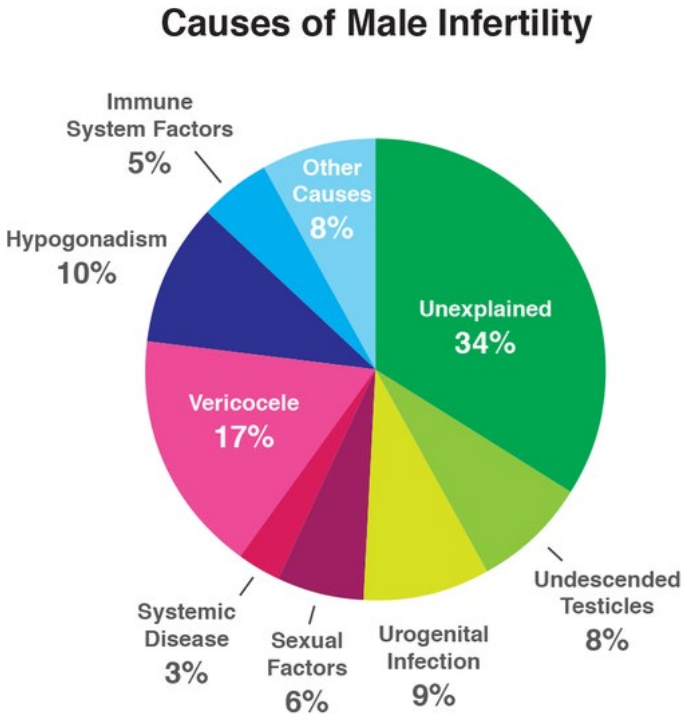
- IVG is a transformative advancement in reproductive biology.
- Recent progress has brought IVG closer to clinical application.
- There is a need to educate IVF professionals and clinicians on IVG's potential impact and future integration into practice.

Expected Learning Outcomes:

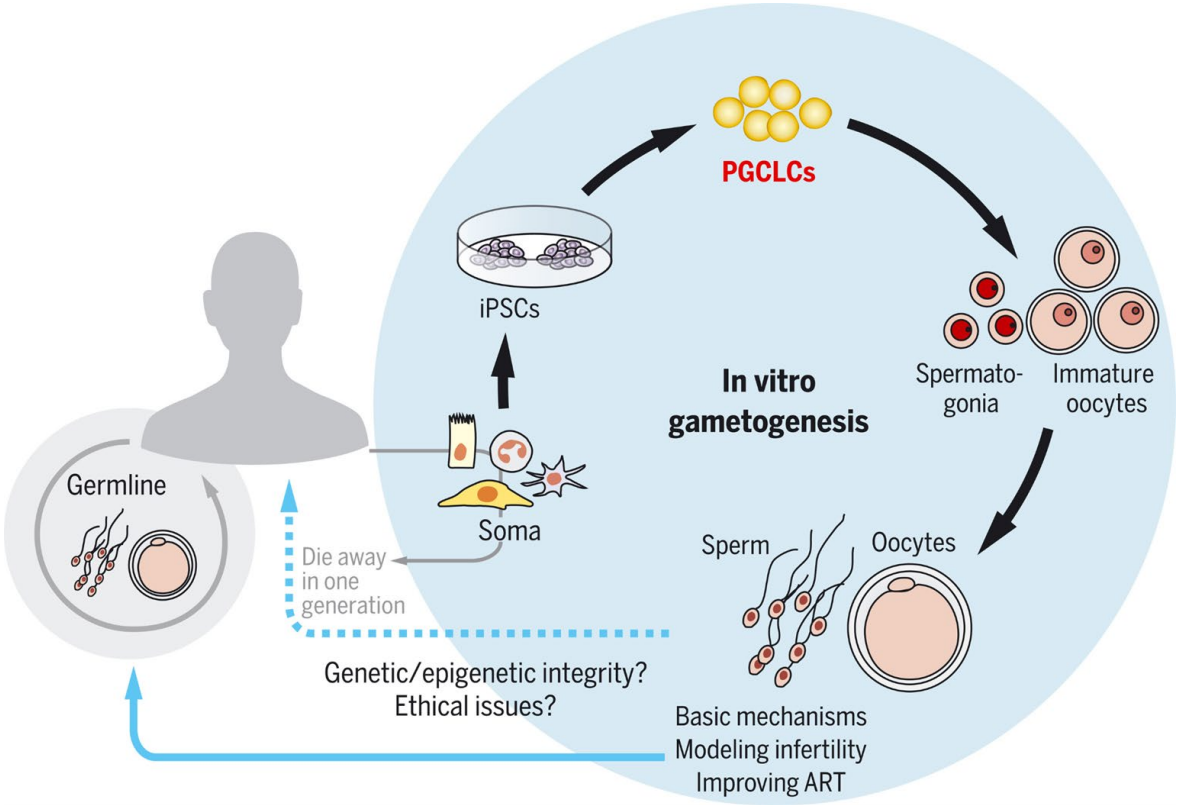
- Describe the current state and key advancements in IVG research.
- Identify the major scientific bottlenecks in IVG development.
- Analyze initial considerations for IVG regulatory frameworks.

Infertility has many causes



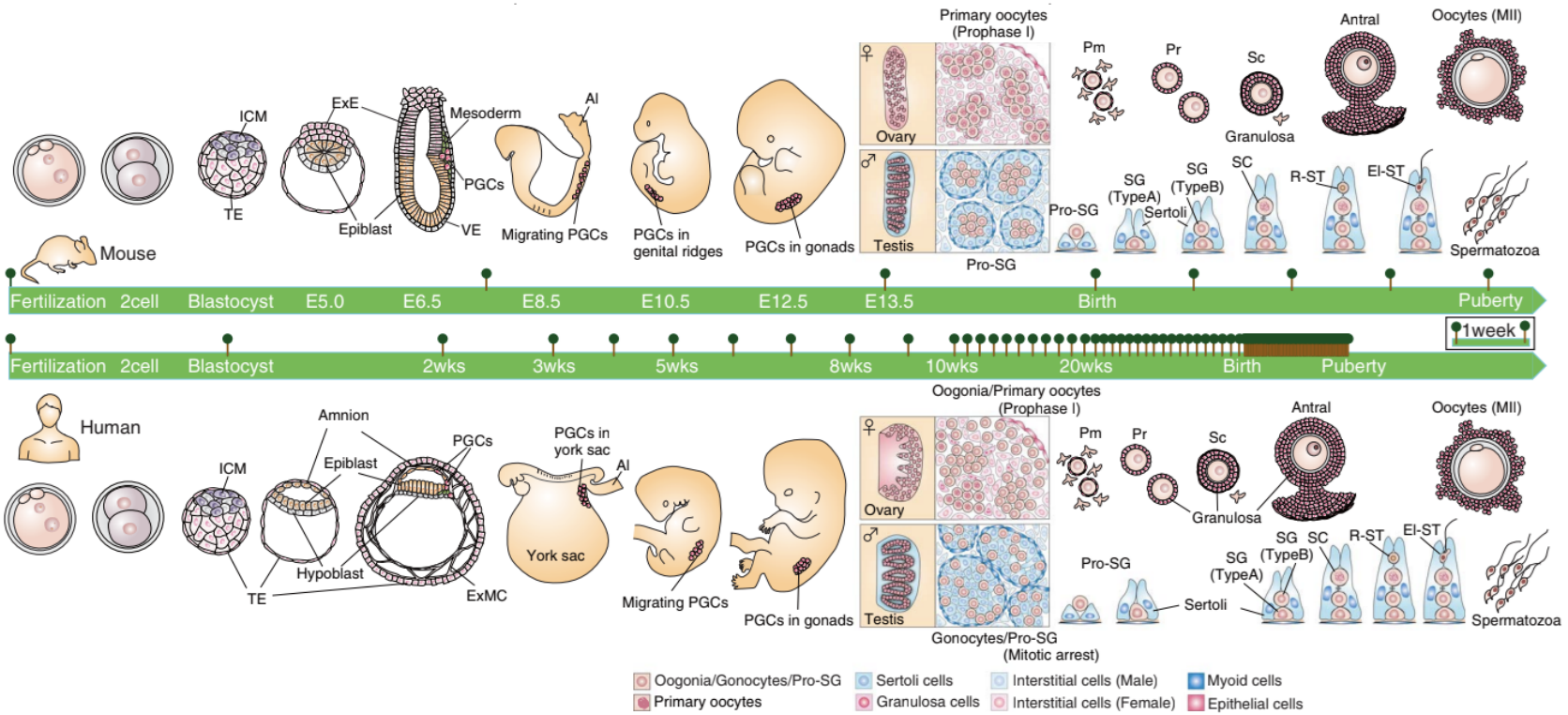


IVG - A single technology to solve the majority of infertility issues



Review: Saitou and Hayashi 2021

Germ cells are probably the most complex cell type



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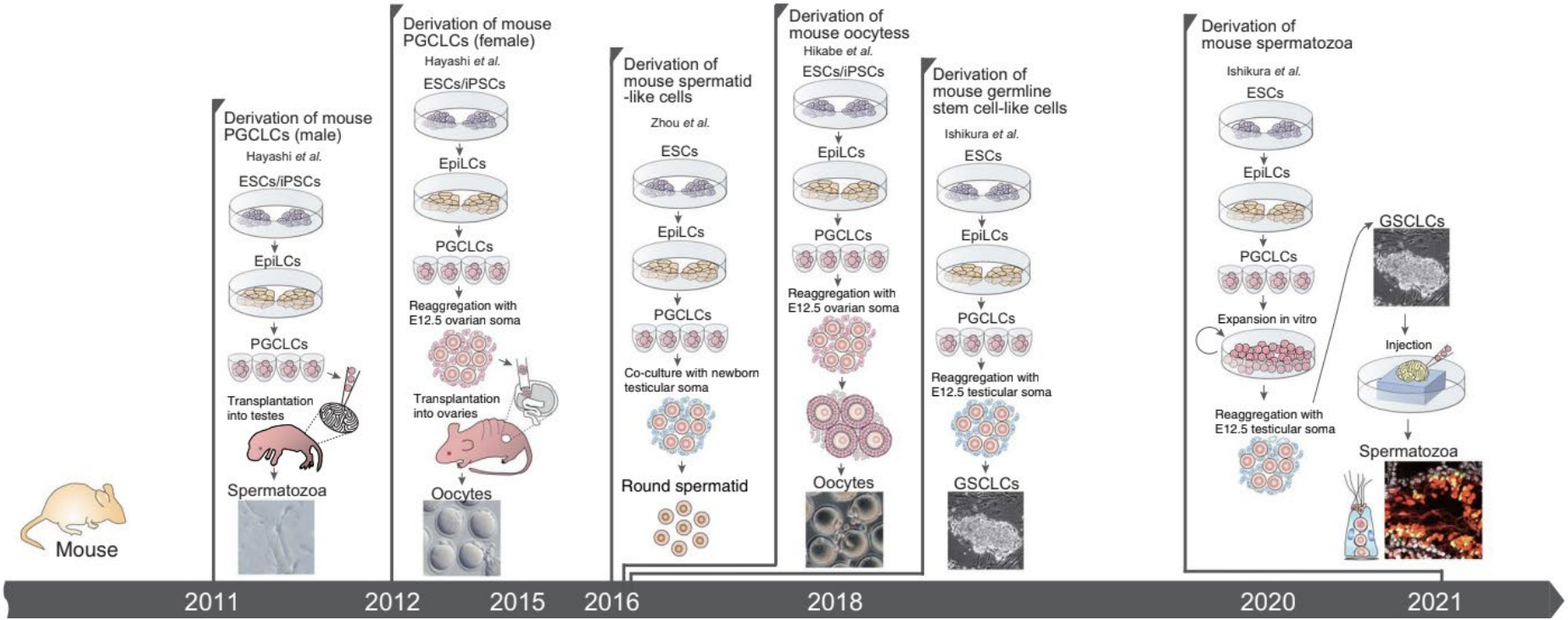
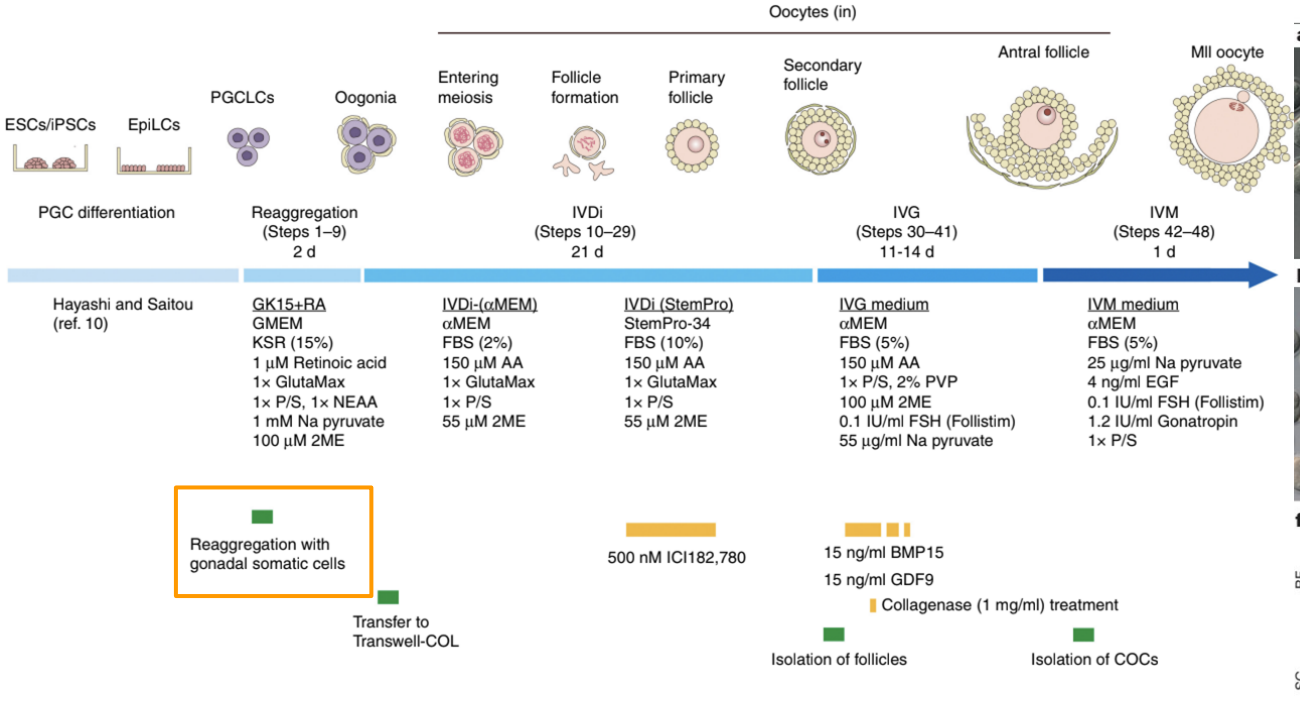
The story of mouse IVG

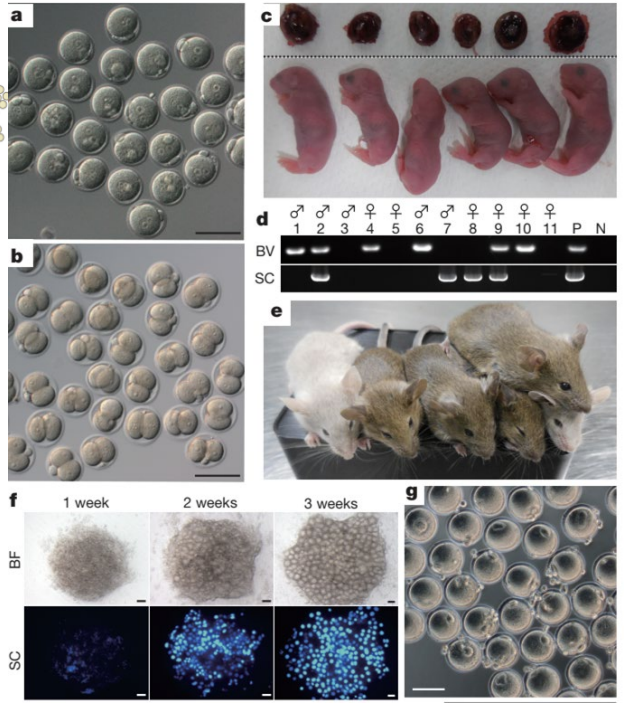
Over 15 years of research progressing mPSCs into eggs and sperm



Adapted from Saitou and Hayashi 2021

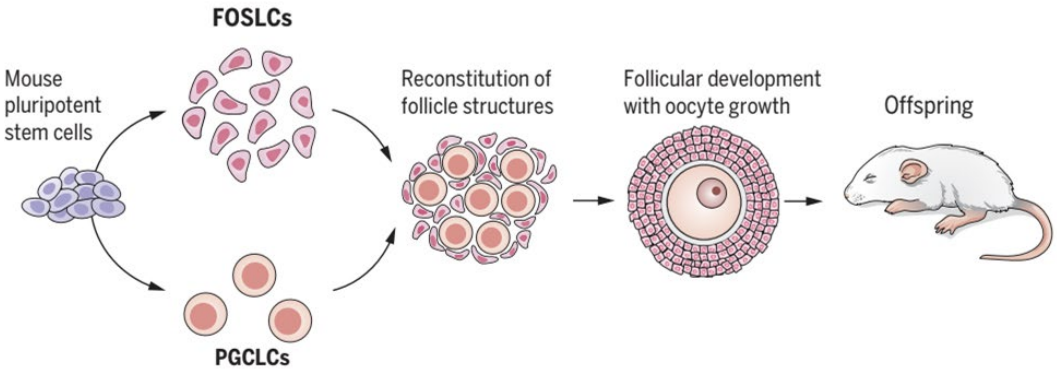
Generation of eggs

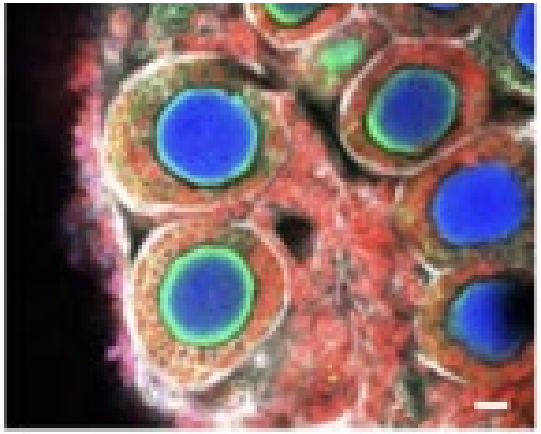


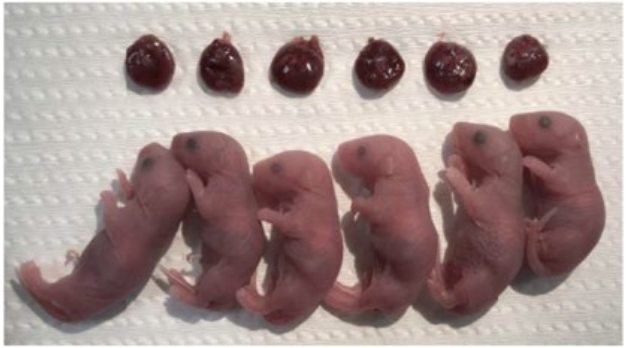


Hikabe et al., 2016 and Hayashi et al., 2017

Generating the ovarian somatic compartment in vitro

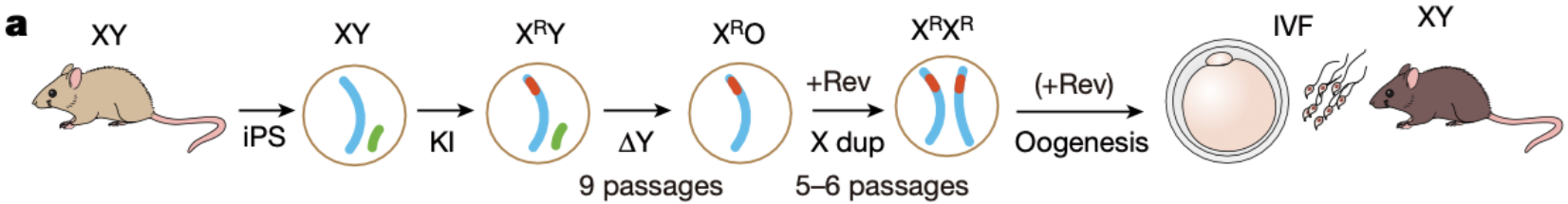


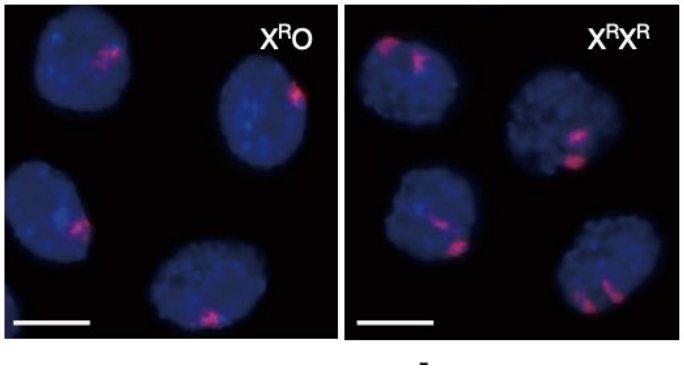


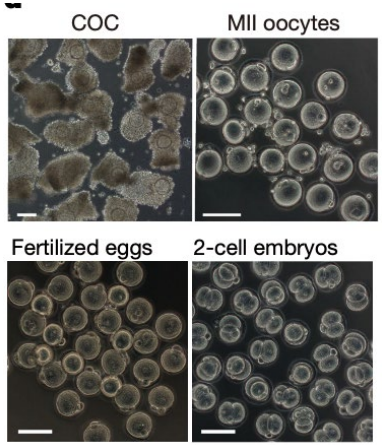


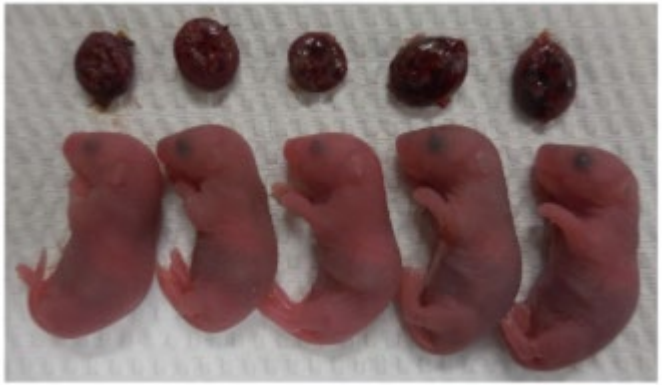
Yoshino et al., 2021

Functional oocytes from male iPSCs



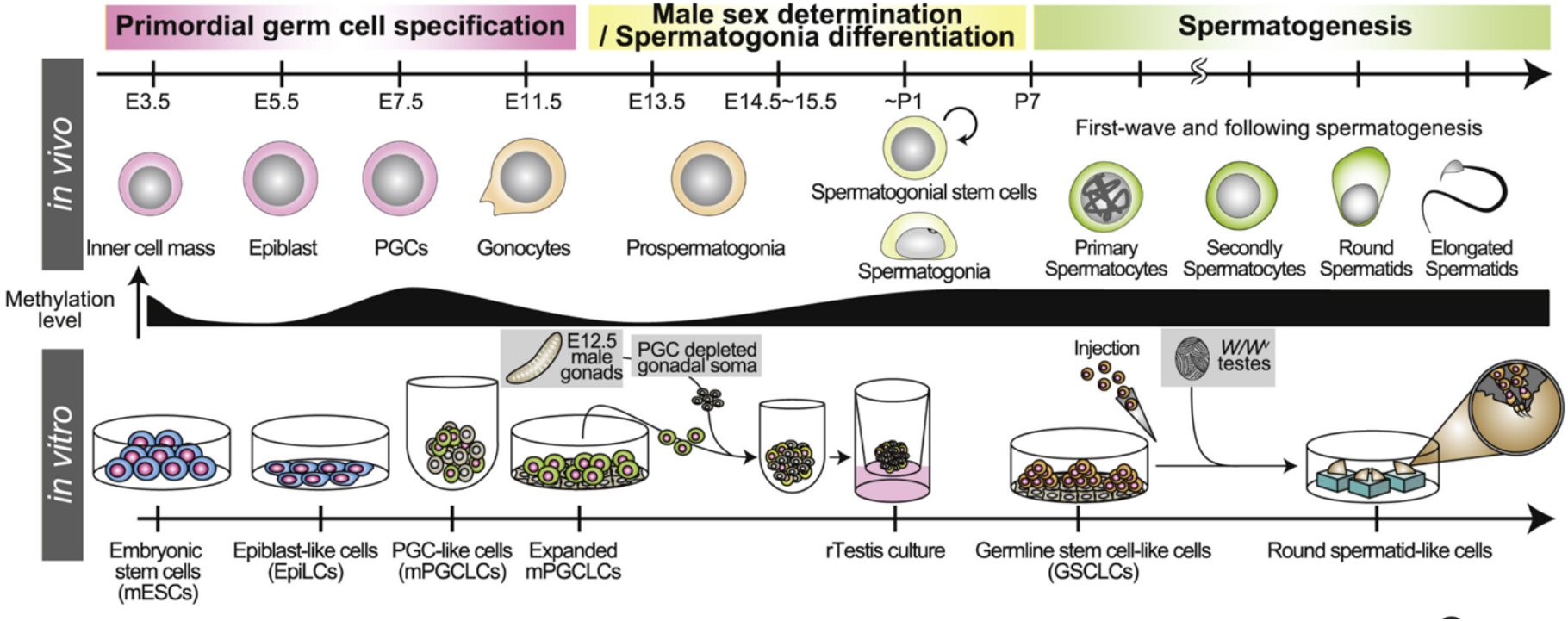






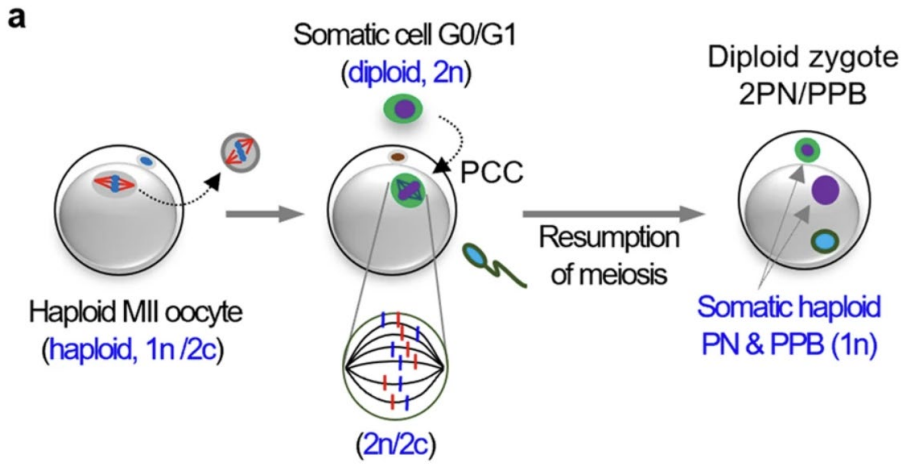
Murakami et al., 2023

Generation of round spermatid-like cells from mESCs



Ishikura et al., 2021

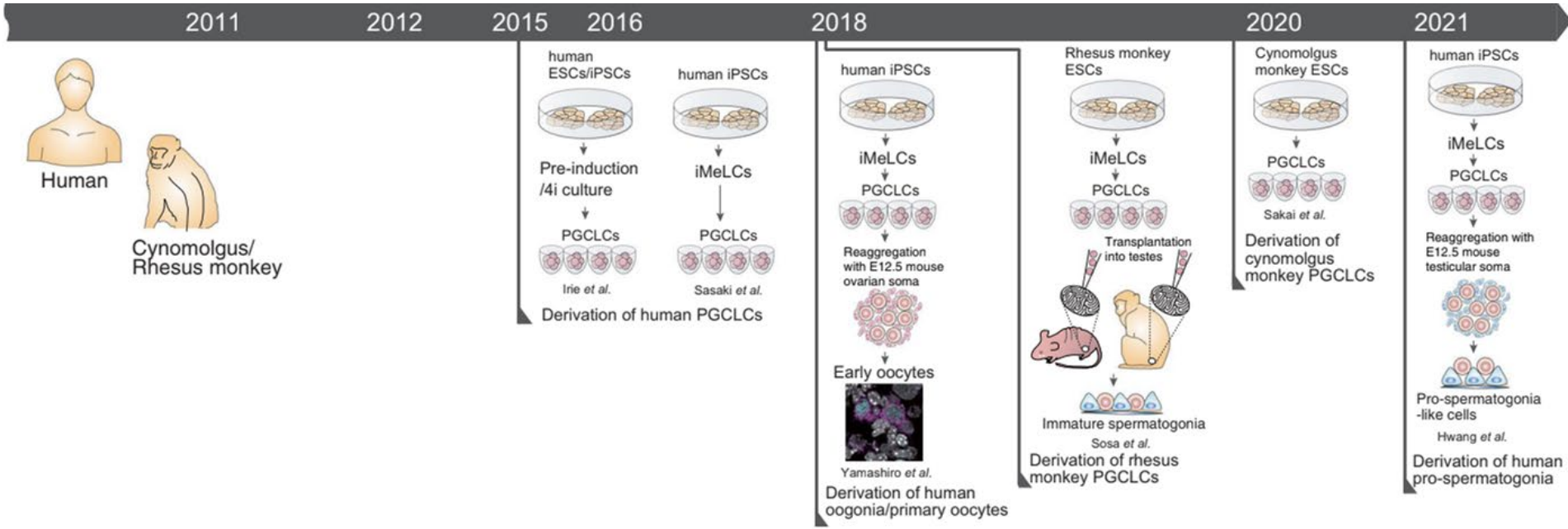
Haploidy in somatic cells induced by mature oocytes



Lee et al., 2022

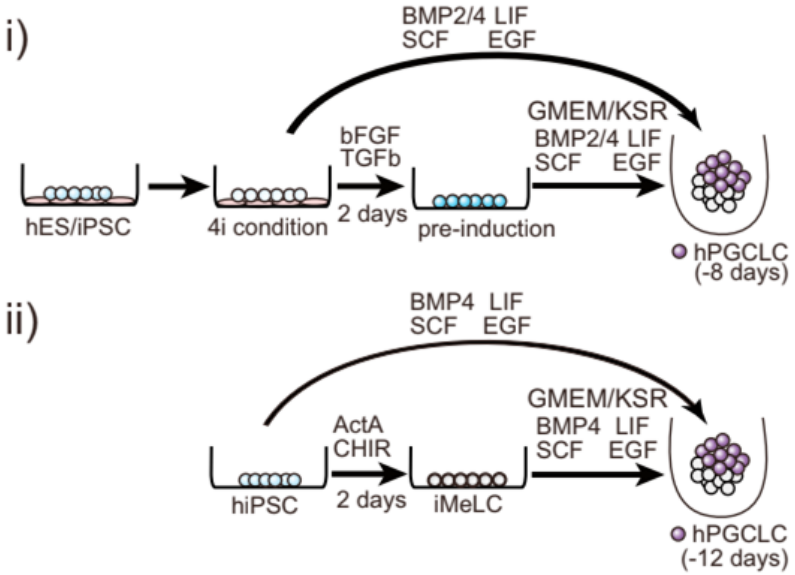
The story of Human IVG

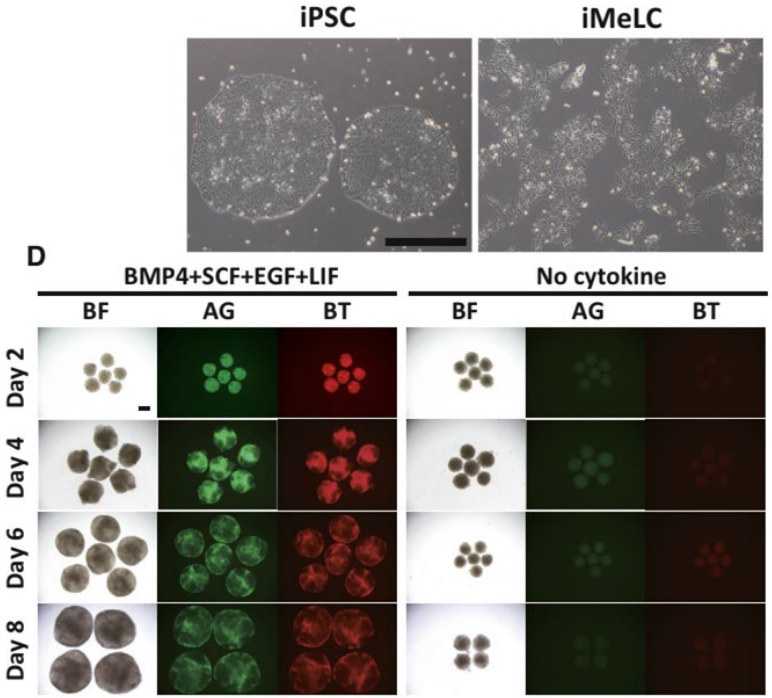
Over 15 years of research progressing iPSC into eggs and sperm



Adapted from Saitou and Hayashi 2021

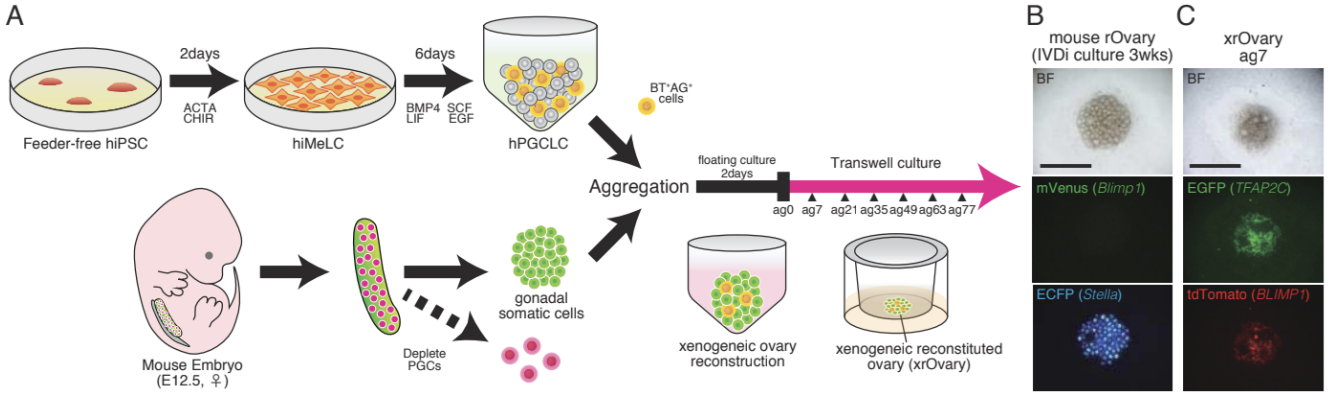
Generation of hPGCLCs in vitro

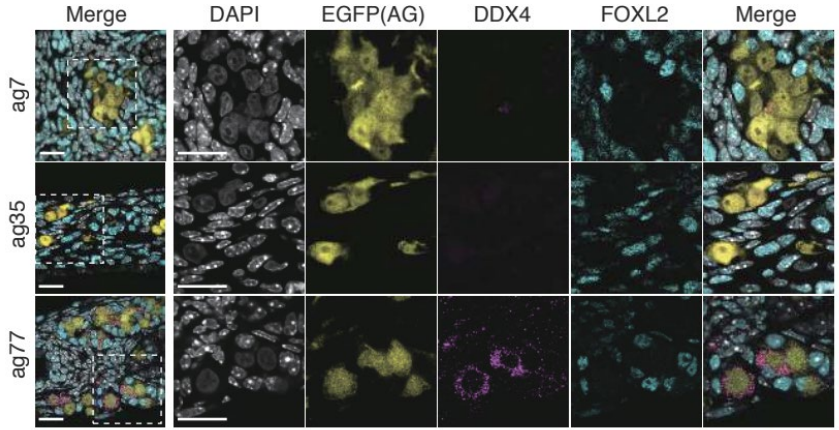




Irie et al., 2015 and Sasaki et al., 2015

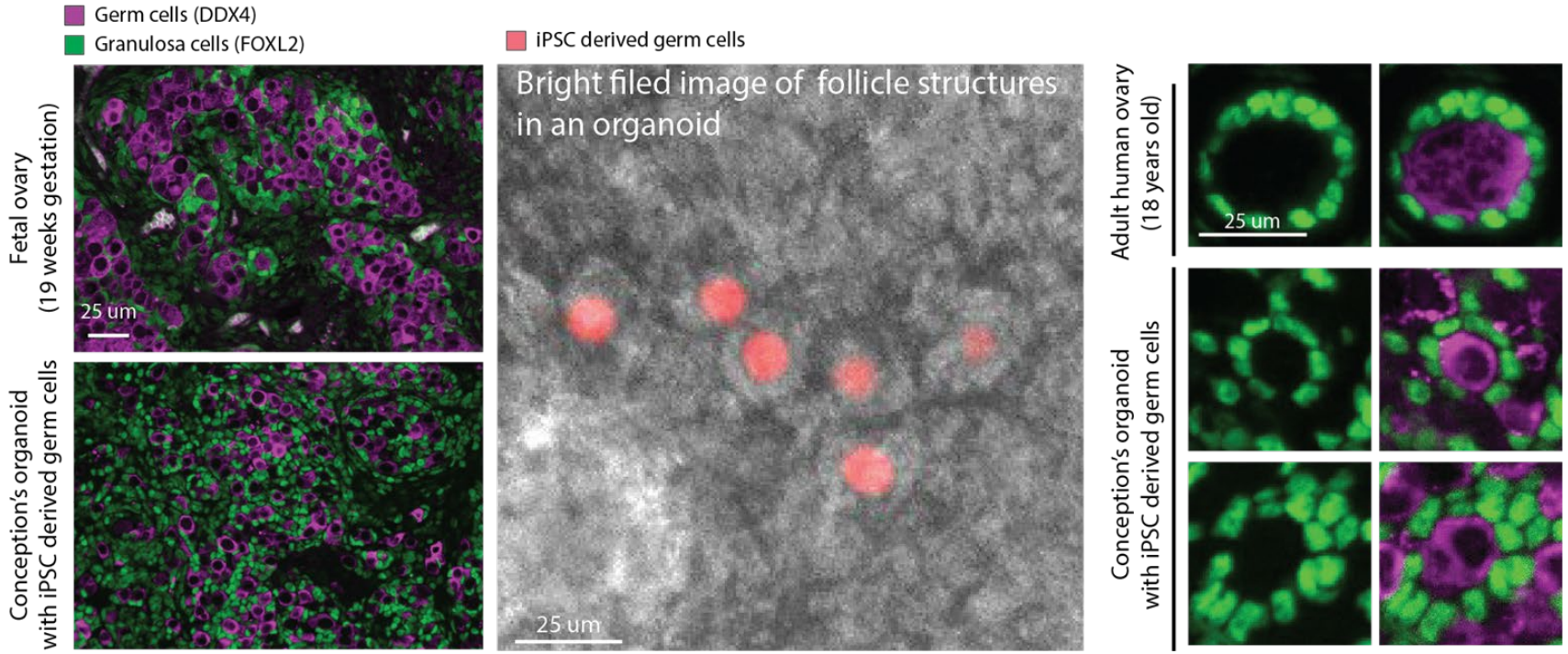
Progressing hPGCLC into oogonia stage





Yamashiro et al., 2018

Generating follicles from hPGCLCs - closing the gap



Conception, unpublished

Scientific challenges for human IVG

- Length of the cultures
- Following all the biological steps
  - Many of these cells might be skipping some important events of gametogenesis
- Epigenetics
  - Germ cells have to go through whole genome epigenetic reprogramming
  - In vitro culture can affect epigenetics
- General low efficiency
  - Lots of optimization to do
- Embryos need to be PERFECT
  - We cannot accept risk when generating new life

How can we make sure everything goes right?

- Animal safety data
  - Mouse
  - NHP
- Human studies
  - Many steps of the process can be studied in depth, but studying the embryo is the ultimate goal
  - We can learn from the IVF field
    - Intrinsic check points
    - Embryo morphology
    - Embryo biopsies + sequencing

Already thinking concretely about how to measure pre-clinical safety

- Making the first proof of concept egg is not 10 years off - we think could be in the next 1-2 years

- Proof of concept won't be ready for implantation - years of in vitro optimization, QC development, and animal/safety testing of course must follow

- What are the specific benchmarks that IVG must meet to be eventually considered for human trials?

We can do extensive pre-clinical characterization in vitro

- Full understanding of the embryo quality:
  - Genetic sequencing
  - RNA sequencing
  - Epigenetic profiling
  - Morphological analysis

- IVG specific benchmarks:
  - Proper epigenetic resets
  - Meiosis occurring normally
  - Mitochondria studies

- Compare IVG generated embryos with traditional IVF embryos (gold standard in medicine for embryos to develop in culture for 5-6 days before transplant)

Animal models can help us determining safety

- in-depth mouse IVG health data could be very valuable:
  - Multi generational studies
  - Genetic integrity

- Non-human primates might be the closest model to human

- What are ultimately the critical animal models?

If it is safe, many people could benefit profoundly

- Conception receives 2-3 emails every week from young cancer survivors, women who have gone through multiple IVF cycles without success, same sex couples dreaming to have children, and more

- The stories they share with us are incredible — this is the most important thing to many of them in their lives

If approved clinically, envision working with existing IVF clinics on this

- IVF clinics would take blood or skin samples from patients and send them to us – we would make eggs and/or embryos to send back

- Implantation procedures would occur as normal with IVF

- Could potentially enable much wider use of PGT-P given could create an higher number of eggs

In the meantime, we could use your help!

- Access to human eggs that are not needed

- Access to human embryos that are no longer wanted

Very helpful for us to characterize and sequence healthy eggs/embryos – come speak with me if would like to explore collaborating

Questions?